

# ADVANCED ORGANIC CHEMISTRY

REACTIONS,  
MECHANISMS, AND  
STRUCTURE

**FOURTH EDITION**

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A Wiley-Interscience Publication

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**Library of Congress Cataloging in Publication Data:**

March, Jerry, 1929—  
Advanced organic chemistry : reactions, mechanisms, and structure  
/ Jerry March. — 4th ed.  
p. cm.

"A Wiley-Interscience publication."  
Includes bibliographical references and indexes.  
ISBN 0-471-60186-2 (alk. paper)  
1. Chemistry. Organic. I. Title.

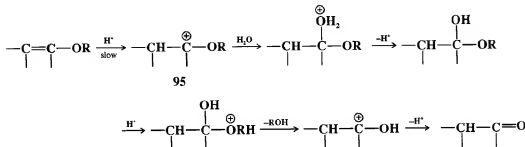
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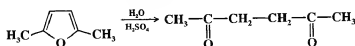
Printed in the United States of America

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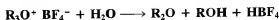
Enol ethers are readily hydrolyzed by acids; the rate-determining step is protonation of the substrate. However, protonation does not take place at the oxygen but at the  $\beta$  carbon,<sup>495</sup> because that gives rise to the stable carbocation **95**.<sup>496</sup> After that the mechanism is similar to the A1 mechanism given above for the hydrolysis of acetals.



Among the facts supporting this mechanism (which is an A- $\text{S}_{\text{E}}2$  mechanism because the substrate is protonated in the rate-determining step) are: (1)  $^{18}\text{O}$  labeling shows that in  $\text{ROCH}=\text{CH}_2$  it is the vinyl-oxygen bond and not the RO bond that cleaves;<sup>497</sup> (2) the reaction is subject to general acid catalysis;<sup>498</sup> (3) there is a solvent isotope effect when  $\text{D}_2\text{O}$  is used.<sup>498</sup> Enamines are also hydrolyzed by acids (see 6-2); the mechanism is similar. Ketene dithioacetals  $\text{R}_2\text{C}=\text{C}(\text{SR}')_2$  also hydrolyze by a similar mechanism, except that the initial protonation step is partially reversible.<sup>499</sup> Furans represent a special case of enol ethers that are cleaved by acid to give 1,4 diones. Thus



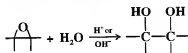
Oxonium ions are cleaved by water to give an alcohol and an ether:



OS I, 67, 205; II, 302, 305, 323; III, 37, 127, 465, 470, 536, 541, 641, 701, 731, 800; IV, 302, 499, 660, 816, 903; V, 91, 292, 294, 703, 716, 937, 967, 1088; VI, 64, 109, 312, 316, 361, 448, 496, 683, 869, 893, 905, 996; VII, 12, 162, 241, 249, 251, 263, 271, 287, 381, 495; 68, 25, 92; 69, 31, 55, 148.

### 0-7 Hydrolysis of Epoxides

#### (3) OC-seco-hydroxy-de-alkoxy-substitution



<sup>495</sup>Jones; Wood *J. Chem. Soc.* **1964**, 5400; Okuyama; Fueno; Furukawa *Bull. Chem. Soc. Jpn.* **1970**, 43, 3256; Kreevoy; Eliason *J. Phys. Chem.* **1969**, 72, 1313; Lienhard; Wang *J. Am. Chem. Soc.* **1969**, 91, 1146; Kresge; Chen *J. Am. Chem. Soc.* **1972**, 94, 2818; Burt; Chiang; Kresge; Szilagyi *Can. J. Chem.* **1964**, 62, 74.

<sup>496</sup>See Chwang; Kresge; Wiseman *J. Am. Chem. Soc.* **1979**, 101, 6972.

<sup>497</sup>Kiprianova; Reksheva *Dokl. Akad. Nauk SSSR* **1962**, 142, 589.

<sup>498</sup>Fife *J. Am. Chem. Soc.* **1965**, 87, 1084; Salomaa; Kankaanperä; Lajunen *Acta Chem. Scand.* **1966**, 20, 1790; Kresge; Chiang *J. Chem. Soc. B* **1967**, 53, 58; Kresge; Yin *Can. J. Chem.* **1987**, 65, 1753.

<sup>499</sup>For a review, see Okuyama *Acc. Chem. Res.* **1986**, 19, 370-376.

The hydrolysis of epoxides is catalyzed by acid catalysts the reaction with this reagent.<sup>500</sup> epoxides.<sup>501</sup>

OS V, 414.

### B. Attack by OH<sup>-</sup>

#### 0-8 Hydrolysis of Hydroxy-de-halides

Acyl halides are hydrolyzed by water. Consequently, water is a difficult case hydrolysis because acyl halides are highly polar solvents. The mechanism is in highly polar solvents for the  $\text{S}_{\text{N}}2$  mechanism.

Hydrolysis of acyl halides where hydrogen bonds are formed.<sup>502</sup> OS II, 74.

#### 0-9 Hydrolysis of Hydroxy-de-alk

R-C-

O

Anhydrides are usually a strong acid catalysts does to can also be catalyzed by bases can also catalyze is actually the results catalyzes the hydrolysis

<sup>500</sup>Fieser; Fieser *Reagents*

<sup>501</sup>Berti; Macchia; Macchia

<sup>502</sup>For a review, see with water, alcohols, and

177-230.

<sup>503</sup>Bender; Chen *J. Am. Chem. Soc.* **1970**, 92, 280-287.

<sup>504</sup>Bentley; Koo; Norman *J. Am. Chem. Soc.* **1970**, 92, 280-287.

<sup>505</sup>Perkin *Trans.* **2** **1989**, 127.

<sup>506</sup>Boyan; Hudson *J. Org. Chem.* **1987**, 52, 197.

<sup>507</sup>Butler; Gold *J. Chem. Phys.* **1935**, 3, 107.

<sup>508</sup>Butler; Gold *J. Chem. Phys.* **1935**, 3, 107.

$$\text{E}_1: \quad \text{---} \text{C} \text{---} \xrightarrow{-\text{H}^+} \text{---} \underset{\text{OH}}{\text{C}} \text{---} \text{OR}$$
$$\text{H}-\overset{\text{OH}}{\underset{|}{\text{C}}}-\text{OH} \xrightarrow{-\text{H}^+} \text{H}-\underset{|}{\text{C}}=\text{O}$$

an  $A_{AC}2$  mechanism because the  $\text{C}_2$ - $^{18}\text{O}$  labeling shows that the  $\text{C}_2$ - $\text{C}_1$  bond that cleaves;<sup>27</sup> (2) the  $\text{C}_2$  isotope effect when  $\text{D}_2\text{O}$  is the mechanism is similar. Ketene mechanism except that the initial  $\text{C}_2$  is a terminal base of enol ethers that

$$\text{H}_2 - \text{CH}_2 - \underset{\text{O}}{\text{C}} - \text{CH}_2$$

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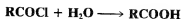
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*(continued)*

OS V, 414.

### 0-8 Hydrolysis of Acyl Halides



Hydrolysis of acyl halides is not usually catalyzed by acids, except for acyl fluorides, where hydrogen bonding can assist in the removal of  $F^{-}$ .<sup>505</sup>

### Hydroxy-de-acyloxy-substitution



Anhydrides are somewhat more difficult to hydrolyze than acyl halides, but here too water is usually a strong enough nucleophile. The mechanism is usually tetrahedral. Only under acid catalysis does the S<sub>N</sub>1 mechanism occur and seldom even then.<sup>369</sup> Anhydride hydrolysis can also be catalyzed by bases. Of course, OH<sup>-</sup> attacks more readily than water, but other bases can also catalyze the reaction. This phenomenon, called *nucleophilic catalysis* (p. 334), is actually the result of two successive tetrahedral mechanisms. For example, pyridine catalyzes the hydrolysis of acetic anhydride in this manner.<sup>367</sup>

<sup>500</sup>Fieser; *Fieser Reagents for Organic Synthesis*, vol. 1; Wiley: New York, 1967, p. 796.

<sup>801</sup>Berti; Macchia; Macchia *Tetrahedron Lett.* **1965**, 3421.

<sup>502</sup>For a review, see Talbot, Ref. 197, pp. 226-257. For a review of the mechanisms of reactions of acyl halides with water, alcohols, and amines, see Kivinen, in Patai *The Chemistry of Acyl Halides*; Wiley: New York, 1972, pp. 177-230.

Bentley; Koo; Norman *J. Org. Chem.* **1991**, 56, 1604.

<sup>504</sup>Bentley; Carter; Harris, Ref. 198; Guthrie; Pike, Ref. 198. See also Lee; Sung; Uhm; Ryu *J. Chem. Soc., Perkin Trans. 2* **1989**, 1697.

<sup>505</sup>Bevan; Hudson *J. Chem. Soc.* **1953**, 2187; Satchell *J. Chem. Soc.* **1963**, 555.

<sup>50a</sup> Satchell *J. Chem. Soc. Rev., Chem. Soc.* **1963**, *17*, 160-203, pp. 172-173. For a review of the mechanism, see Talbot, *Ref.* 197, pp. 280-287.

<sup>56</sup> Butler; Gold *J. Chem. Soc.* **1961**, 4362; Fersht; Jencks *J. Am. Chem. Soc.* **1970**, 92, 5432, 5442; Deady; Finlayson *Aust. J. Chem.* **1983**, 36, 1951.